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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,603	06/08/2005	Tatsuhiko Kodama	14875-137US1	5647

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EXAMINER	
LIETO, LOUIS D	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/516,603	KODAMA ET AL.	
	Examiner	Art Unit	
	Louis D. Lieto	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-3,10-18 and 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-9 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/13/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response to the Restriction requirement was received on 3/29/2006. Claims 1-20 are pending in the instant application. Applicant's election without traverse of Group II, claims 4-9 and 19 drawn to a method for producing an antibody that recognizes a target antigen, comprising producing a transgenic non-human animal and immunizing the non-human animal is acknowledged.

Claims 1-3, 10-18 and 20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/29/06.

Claims 4-9 and 19 are currently under consideration.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application, by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

On 6/08/05 applicant filed a sheet labeled: The Combined declaration and Power of Attorney. However, only the signature sheet (2 of 2) was received. Applicant is required to submit a complete Oath declaration including both a full body and a signature sheet.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement filed 3/25/05 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

Claim 4 is objected to because of the following informalities: The claim is drawn to a gene expressibly encoding the background antigen. These phrases are redundant, since encoding and expressibly have the same meaning in the context of this claim. It is suggested that the claim be amended to delete the term expressibly. Appropriate correction is required.

Claim 19 is objected to because of the following informalities: The claim is drawn to an animal that expressibly comprises a gene encoding a baculovirus membrane protein gp64. This phrasing is redundant since encoding and expressibly have the same meaning in the context of this claim. It is suggested that the claim be amended to delete the term expressibly. Appropriate correction is required.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Specifically, Figure 4 of the drawings includes sections labeled 30, 34, 46 and normal, however there is no explanation as to what these labels signify in the brief description of the drawings. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-9 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for producing an antibody against an antigen, wherein the method comprises the steps of:

(a) preparing a baculovirus that comprises a DNA which encodes an antigen or an epitope thereof;
(b) infecting a host cell with the baculovirus of (a) to obtain a budding virus that expresses said antigen or an epitope thereof;;
(c) producing a transgenic mouse that expresses a gene encoding the baculovirus membrane protein gp64,
(d) immunizing the transgenic non-human mouse of (c) with a fraction comprising the budding virus of (b); and
(e) recovering an antibody-specific for said antigen from the immunized animal.

, does not reasonably provide enablement for

A method for producing an antibody against a target antigen, wherein the method comprises the steps of:
(a) preparing an immunogen comprising the target antigen and any background antigen;
(b) producing any transgenic non-human animal comprising a gene expressibly encoding any background antigen;
(c) administering the immunogen of (a) to the transgenic non-human animal of (b); and
(d) isolating the antibody against the target antigen from the transgenic non-human animal.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims..

The claims are drawn to a:
A method for producing an antibody against a target antigen, wherein the method comprises the steps of:
(a) preparing an immunogen comprising the target antigen and any background antigen;
(b) producing any transgenic non-human animal comprising a gene expressibly encoding any background antigen;
(c) administering the immunogen of (a) to the transgenic non-human animal of (b); and
(d) isolating the antibody against the target antigen from the transgenic non-human animal.

The claims broadly encompass producing any transgenic non-human animal encoding any background antigen. However the specification only provides guidance on making a transgenic mouse that expresses 64 (Specification examples 1-5). The art of making transgenic animals other is generally unpredictable. Houdebine et al., states that "numerous experiments have shown that the level and specificity of expression of a gene construct used as a transgene

cannot be easily predicted" {Houdebine et al. (2000) Transgenic Research 9:305-320; pg. 309, col. 2:The expression of transgenes}. Further, Houdebine et al. states that the potency of any transgene can only be estimated in transgenic animals and the level of expression of transgenes in mice is not predictive of their levels in other animals (pg. 310, col. 1, pgph 2). Finally, Houdebine et al. states that another well known problem with transgenesis is leaky expression of the transgene in various tissues in which the utilized promoter is not expected to work because of ectopic expression due to a position effect (pg. 310, col.1, pgph 3). See also Kolb et al., who states that "the expression of foreign genes in transgenic animals is generally unpredictable as transgenes integrated at random after pro-nuclear injection into fertilized oocytes" because of inhibition by neighboring chromatin {Kolb et al. (1999) Gene 227:21-31; Abstract}. The phenotype produced by a specific transgene was not predictable in different species at the time of filing. As Murray states, "the observation that the oMT1a-oGH transgene that is regulated in mice is uncontrollable in both sheep and pigs suggests that transgene constructs still need to be tested in the species of interest." {Murray (1999) Theriogenology 51:149-159; pg. 150, pgph 4}. Sigmund, C., concurs, reporting that variation in the genetic background contributes to the unpredictability of the resulting phenotypes of transgenic or gene-targeted animals {Sigmund, C., (2000) Arterioscler. Thromb. Vasc. Biol., p. 1425-1429}. "Animals containing the same exact genetic manipulation exhibit profoundly different phenotypes when present on diverse genetic backgrounds, demonstrating that genes unrelated, per se, to the ones being targeted can play a significant role in the observed phenotype" (e.g. abstract).

Further, the art of making any transgenic mouse, other than the disclosed mouse, is not predictable because of several factors. Well-regulated transgene expression is the key to

successful transgenic work, but all too often experiments are blighted by poor levels or the complete absence of expression, as well as less common problems, such as leaky expression in non-targeted tissues. A feature common to many transgenic experiments is the unpredictable transgenic lines produced with the same construct frequently displaying different levels of expression. Sigmund states that in regards to mice "many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studied...Although all mouse strains contain the same collection of genes, it is allelic variation...and the interaction between allelic variants that influence a particular phenotype." (pg, 1425, col. 1, Introduction). These "epigenetic" effects can dramatically alter the observed phenotype and therefore can influence or alter the conclusions drawn from experiments" (e.g. introduction). Sigmund concludes by stating that "in the absence of inbred strains, there is no optimal set of experimental and control conditions that normalizes the epigenetic effects of unlinked loci," and that each transgenic mouse strain must be assessed as to whether the phenotype observed is due specifically to the targeted modification or is affected by other loci (pg. 1428, col. 1, Guidelines). This is due in part to the fact that expression levels do not always correlate with the number of transgene copies integrated {Leiter et al. (2002) Diabetologia 45:296-308;pg. 304, col. 1}. Such copy- number-independent expression patterns emphasize the influence of surrounding chromatin on the transgene (pg. 303, col. 2). Additionally, promoters and enhancer elements may not function in any species because they may require specific cellular factors. The genotype of the mouse strain used can have a drastic effect on the phenotype of a transgenic mouse. Lariviere et al. teaches that the 129 and C57BL/6 mouse strains, despite having the same null mutation "display significant and sometimes extreme phenotypic

differences." {Lariviere et al. (2001) J. Pharm. And Exp. Therap. 297:467:473; Abstract}. Here, the claims broadly encompass making any transgenic non-human animal that is transgenic for any background antigen. Given the teachings in the specification and the general unpredictability in the art the skilled practitioner would be unable to make any transgenic animal for use in the claimed invention, except a transgenic mouse that expresses a gene encoding the baculovirus membrane protein gp64, without undue and extensive experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4,5, 7-9 rejected under 35 U.S.C. 102(a) as being anticipated by Tsuchiya M. (1.21.2003) Therapeutic Antibody Presentation, pgs. 1-21.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Tsuchiya M. provides guidance on the immunization of a mouse transgenic for a gp64 with a budded virus comprising transmembrane target antigen and a background antigen, and the isolation of an antibody against the target antigen (pg. 14). Thus, by teaching all the limitations of the claims as written, Tsuchiya M. anticipates the instant invention as claimed.

Claims 4,5 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Mancini et al. {Mancini et al. (1993) J. Med. Virol 39 : 67-74}.

Mancini et al. provides guidance on the immunization of a mouse transgenic for a background antigen with an immunogen comprising a target antigen and a background antigen, and the isolation of antibody against the target antigen (Abstract). Specifically, Mancini et al. teaches a mouse transgenic for viral antigen HbsAg, which does not produce antibodies to this antigen (Abstract). Further, Mancini et al. teaches the immunization of the mouse with recombinant HbsAg viral particles comprising an HIV envelope protein. The mouse develops antibodies to the HIV protein (Abstract). Serum was collected by retroorbital puncture and HIV specific antibodies were isolated by binding to HIV specific peptides (pg. 68, col.2- pg. 69, col. 1). Thus, by teaching all the limitations of the claims as written, Mancini et al. anticipates the instant invention as claimed.

No claims allowed

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Lou Lieto whose telephone number is (571) 272-2932. The examiner can normally be reached on Monday-Friday, 9am-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Patent applicants with problems or questions regarding electronic images that

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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